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EXAMINER
SWITZER, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/091,841	CHO ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-49,65-70 and 73-94* is/are pending in the application.

4a) Of the above claim(s) *47-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-46,65-70 and 73-94* is/are rejected.

7)☒ Claim(s) *29-46,65-70 and 73-94* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 March 2002* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: IDS filed 3/5/02, 6/10/02, 7/15/02.

DETAILED ACTION

The preliminary amendment filed 3/5/02 amending the specification and claims has been entered. Claims 1-28, 50-64 and 71-72 were cancelled and claims 73-94 were added. The pending claims are subject to a restriction requirement as follows.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 29-46, 65-70, and 73-94, drawn to nucleic acids, vectors, host cells, plants, seeds, and methods of expressing polypeptides, classified in class 536, subclass 23.1, for example.

   II. Claims 47-49, drawn to polypeptides, classified in class 435, subclass 189.

The inventions are distinct, each from the other because of the following reasons:

The nucleic acids and constructs of invention I and the polypeptides of invention II are patentably distinct in structure and physiochemical properties. Invention I is drawn to nucleic acids and constructs comprising nucleic acids whereas invention II is drawn to proteins. Because nucleic acids are composed of nucleotides and proteins are composed of amino acids, the inventions have different structural and functional properties. Furthermore, the compositions are utilized in different methodologies, such that nucleic acids may be utilized in hybridization assays, while proteins may be used in ligand binding assays or to generate antibodies. Synthesis of the proteins of invention II do not require the particular nucleic acids of invention I since the proteins of invention II can be isolated from natural sources or chemically synthesized. Thus, even insofar as invention I includes methods of expressing polypeptides using the nucleic acids and constructs within invention I (i.e. a method of making the proteins of invention II), the

inventions are still distinct because the polypeptides of invention II can be made by a materially different method, as noted.

2. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as demonstrated by their different classification and recognized divergent subject matter and because inventions I-II require different searches that are not coextensive, examination of these claims would pose a serious burden on the examiner and therefore restriction for examination purposes as indicated is proper.

3. During a telephone conversation with Michael Ward on 7/21/03 a provisional election was made with traverse to prosecute the invention of group I, claims 29-46, 65-70, 73-81, and 82-90. Affirmation of this election must be made by applicant in replying to this Office action. Claims 47-49 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code (i.e. see page 16). See MPEP § 608.01.

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of the sequence rules because it does not contain a copy of the sequence listing in paper form. It is noted that at the time of filing, applicant filed a paper requesting the transfer of both the CRF and the paper copy of the sequence listing from parent application 09/540014. The CRF of the parent application has been transferred, but transfer of the paper copy is not provided for by the sequence rules. Consequently, Applicant is required to submit a paper copy of the Sequence Listing and a letter stating that the content of the paper and computer readable copies of the Sequence Listing are the same and, where applicable, include no new matter.

Claim Objections

7. Claims 29-46, 65-70, and 73-94 are objected to because independent claims 29, 32, 32, 65, 67, and 68 all refer to "a sequence set forth in figure 5A." MPEP 2173(s) states "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." In the instant case each of the sequences in figure 5A can be properly represented using a proper sequence identifier.

8. Claim 43 is objected to because it recites "he," which appears to be a typographical error and should be "the."

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 29-46, 65-70, and 73-94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims all refer to "a sequence complementary to that set forth in Figure 5A," or "comprising a nucleic acid sequence set forth in figure 5A" or "having at least 75% identity to a sequence set forth in figure 5A" or "encoding an amino acid sequence set forth in Figure 4" yet figures 4 and 5 recite multiple sequences. It is acknowledged that the claim further recites SEQ ID NO: 10 or SEQ ID NO: 9 in parentheses, but it is unclear if the claim therefore intends to be referring to ANY sequence in figures 1 or 2, preferably SEQ ID NO: 10 or SEQ ID NO: 9, or if the claim intends to refer to only SEQ ID NO: 10 or SEQ ID NO: 9 in particular.

Further, the claims are indefinite over what is intended by the language "a sequence"... "as set forth in Figure..." because it is not clear if the use of the article "a" implies that it can be any sequence or subsequence present within the full length sequences set forth in the figures or if applicant intends that the claims be requiring or referring to the full length of the sequences set forth in the appropriate figures.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-31, 33-46, 65-70, 73-74, 76-77, 79-80, 82-83, 85-86, 88-89, and 91-94 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are drawn to recombinant nucleic acids encoding an NADPH-thioredoxin reductase protein (NTR protein) and compositions comprising these nucleic acids. Claims 29 and 65 are broadly drawn to include any nucleic acid encoding an NTR protein which hybridizes to a sequence complementary to that set forth in figure 5A (SEQ ID NO: 10). These claims do not contain specific functional language. While the claims recite that the nucleic acid encodes an "NTR protein" it is not clear from the language of these claims what functionality the encoded proteins must have. Claims 30 and Claims 66 further limit claims 29 and 65 by reciting that the claimed nucleic acid comprises "a sequence" as set forth in figure 5A (SEQ ID NO: 10). As noted in the 112 2nd rejection, it is not clear from the language of the claims if "a sequence" means the entire sequence as set forth, or if it encompasses a portion of the sequence. Claims 31 and 67 are broadly drawn to include all nucleic acids encoding an NTR protein, where in said nucleic acids comprise nucleic acids with 75% "a sequence" as set forth in figure 5A (SEQ ID NO: 10). Once again, these claims do not include clear functional language to limit or describe the protein encoded by the claimed polynucleotide. Further, even in light of such functional language, the specification does not provide guidance as to how to arrive at sequences which have only 75% identity to SEQ ID NO: 10 (or any of the other sequences recited in figure 5A)

yet still retain the functionality of SEQ ID NO: 10. All of the other rejected claims depend from these independent claims.

The instant specification only describes three nucleic acids which encode NTR proteins, that is a sequence from barley, instant SEQ ID NO: 10 as well as sequences from E. coli and A. thaliana (SEQ ID NO: 25 and 26, respectively).

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of a polynucleotides which encode NTR proteins, wherein the polynucleotides comprise instant SEQ ID NO: 10, 25, and 26. The subject matter which is claimed is described above.

First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed nucleic acids encoding an NTR protein, and encompass such nucleic acids from any plant species, as well as any variants which may that have as little as to 75% identity to SEQ ID NO: 10 (or any of the other nucleic acids in figure 5A). The specification only describes only three nucleic acids encoding a NTR proteins and fails to teach or describe any other NTR proteins encoding polynucleotides. With regard to SEQ ID NO: 10, the specification does not teach any variants or homologues of SEQ ID NO: 10 that also encode NTR proteins (active or inactive proteins). Therefore, there is a lack of guidance or teaching regarding structure and function because there

are minimal examples provided in the specification and because there is no guidance found in the with regard to all of the variation of sequence encompassed within the instant claims.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims, beyond the nucleic acid disclosed as SEQ ID NO: 10, 25, and 26. The specification does not provide any disclosure as to how the instant encoded polypeptides can be modified and still retain the disclosed biological activity. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the SEQ ID NO: 10, 25 and 26 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of any NTR protein encoding nucleic acids which comprises sequences that will hybridize under highly stringent conditions to SEQ ID NO: 10, 25, or 26 or with as little as 75% homology to SEQ ID NO: 10, 25, or 26. Furthermore, this rejection applies to claims 30 and 66 only insofar as these encompass nucleic acids that comprise fragments of the sequences set forth in figure 5A (as discussed in the 112 2nd paragraph rejection). These lack written description insofar as the open "comprising" language along with the "a sequence" language encompasses any nucleic acid that comprises a fragment of the recited sequences within any larger context, encompassing undescribed splice variants, sequences from other organisms, genomic DNA, etc. Claims to an isolated nucleic acid comprising SEQ ID NO: 10, for example, would be properly described.

11. Claims 29-31, 33-46, 65-70, 73-74, 76-77, 79-80, 82-83, 85-86, 88-89, and 91-94 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids, constructs, compositions, and methods which comprise or utilize instant SEQ ID NO: 10, 25 or 26 (in their entirety), as well as a nucleic acid encoding instant SEQ ID NO: 9, 24 or 25, does not reasonably provide enablement for any nucleic acid which hybridizes under high stringency conditions to these nucleic acids, or any nucleic acid that has 75% homology to these nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature of the invention, Breadth of the Claims

These claims are drawn to recombinant nucleic acids encoding an NADPH-thioredoxin reductase protein (NTR protein) and compositions comprising these nucleic acids. Claims 29 and 65 are broadly drawn to include any nucleic acid encoding an NTR protein which hybridizes to a sequence complementary to that set forth in figure 5A (SEQ ID NO: 10). These claims do not contain specific functional language. While the claims recite that the nucleic acid encodes an "NTR protein" it is not clear from the language of these claims what functionality the encoded proteins must have. Claims 30 and Claims 66 further limit claims 29 and 65 by reciting that the claimed nucleic acid comprises "a sequence" as set forth in figure 5A (SEQ ID NO: 10). As noted in the 112 2nd rejection, it is not clear from the language of the claims if "a sequence" means the entire sequence as set forth, or if it encompasses a portion of the sequence. Claims 31 and 67 are broadly drawn to include all nucleic acids encoding an NTR protein, where in said nucleic acids comprise nucleic acids with 75% "a sequence" as set forth in figure 5A (SEQ ID NO: 10). Once again, these claims do not include clear functional language to limit or describe the protein encoded by the claimed polynucleotide. Further, even in light of such functional language, the specification does not provide guidance as to how to arrive at sequences which have only 75% identity to SEQ ID NO: 10 (or any of the other sequences recited in figure 5A) yet still retain the functionality of SEQ ID NO: 10. All of the other rejected claims depend from these independent claims.

State of the Art, Level of Unpredictability

The prior art, as taught by the specification teaches the nucleic acid sequence encoding an NTR protein from both E. coli and from Arabidopsis (SEQ ID NO: 25 and 26 herein). Instant

SEQ ID NO: 10 is a nucleic acid sequence encoding an NTR protein from barley. The prior art does not provide any guidance as to how to modify these nucleic acids yet result in nucleic acids which encodes NTR proteins that retain their oxidoreductase activity.

The level of unpredictability with regard to such modifications is quite high. Enzyme function and activity is intrinsically related to the structure of the enzyme, and even single amino acid changes can alter the functionality of an enzyme. This point is exemplified repeatedly in the prior art, with regard to reductase enzymes in particular. For example, Gilberger *et al.* (The Journal of Biological Chemistry, Vol. 272, No. 47, pages 29584-29589, 1997) teach that changes in the active site of a thioredoxin reductase from Plasmodium either results in total loss of activity or significant loss of activity, depending on the exchanged amino acid (abstract and throughout). Nagai *et al.* (Blood, Vol. 81, No. 3, p. 808-814, 1993) teach a single amino acid change in the NADH cytochrome b5 reductase caused a significant reduction in enzyme activity which explains a patient's hereditary methemoglobinemia. In a third example, Bullerjahn *et al.* (the Journal of Biological Chemistry, Vol. 267, No. 2, p. 864-870, 1992) teach tha tdeletion mutations of a dihydrofolate reductase lost activity and were more unstable than the wild type. Thus, these exemplify, that modifications to encoded enzymes are highly unpredictable and often result in loss of activity.

Working Examples and Direction Provided

The specification does not provide any particular guidance or examples of nucleic acids that are modified with regard to the disclosed sequences, yet the instant claims encompass nucleic acids that encode a widely variant polypeptides considering the changes allowed within the language of the rejected claims.

Conclusion

Thus, in light of the breadth of the claims, the high level of unpredictability in the prior art, the lack of guidance provided in the prior art or the instant specification, and the lack of working examples other than the sequences given in the instant specification, it is concluded that it would require undue experimentation to practice the invention commensurate in scope with the instant claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 29, 30, 31, 32, 33, 34, 35, 41, 42, 46, 65, 66, 67, 68, 73, 74, 75, 76, 77, 78, 91, and 94 are rejected under 35 U.S.C. 102(e) as being anticipated by Lalgudi *et al.* (US 6476212).

Lalgudi *et al.* teach an isolated nucleic acid which has 89.8% local similarity with nucleotides 1-226 of instant SEQ ID NO: 10. Specifically, nucleotides 29-250 of SEQ ID NO: 3512 as taught by Lalgudi *et al.* is 89.8% identical to nucleotides 1-226 of instant SEQ ID NO: 10. An alignment of the two sequences is as follows, the top sequence being SEQ ID NO: 10 and the bottom sequence being SEQ ID NO: 3512 from Lalgudi *et al.*

```
Qy          1 ATGGAGGGATCCGCCGCGGCGCCGCTCCGCACGCGCGTGTGCATCATCGGCAGCGGCCCG 60
              || |||||||||||||| || |||||||||| |||| | |||||||||| ||||| ||
Db         29 ATNGAGGGATCCGCCGCCGCTCCGCTCCGCANGCGCATCTGCATCATCGGGAGCGGTCCC 88
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Qy          61 GCCGCGCACACGGCGGCCATCTACGCGGCCCGCGCGGAGCTCAAGCCCGTGCTCTTCGAG 120
               || |||||||||||  ||||||||||||||||||||||||  |||||||  ||||||||||||
Db          89 GCTGCGCACACGGCAGCCATCTACGCGGCCCGCGCGGAG-TCAAGCCTGTGCTCTTCGAG 147

Qy         121 GGCTGGATGGCCAACGACATCGCCGCGGGGGGCCAGCTCACCACCACCACCGACGTCGAG 180
               |||||  |||||||||||||||||||||| || ||||||||||||||||||||||||||||
Db         148 GGCTG--TGGCCAACGACATCGCCGCGGGCGGGCAGCTCACCACCACCACCGACGTCGAG 205

Qy         181 AACTTCCCCCGGATTCCCCACCGGCATCATGGGCATCGACCTCATGG 226
               || ||||| || ||||||| |||||||||||||  ||||||||||
Db         206 AA-TTCCCGGGCTTCCCCAACGGCATCATGGGCGCCGACCTCATGG 250
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With regard to claims 29 and 65, Lalgudi *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to instant SEQ ID NO: 10. Considering the high level of homology between the nucleotide sequence taught by Lalgudi *et al.* and the portion of instant SEQ ID NO: 10, the sequence taught by Lalgudi *et al.* would be expected to hybridize under high stringency conditions to instant SEQ ID NO: 10. The nucleic acid encoded by the SEQ ID NO: 3512 taught by Lalgudi *et al.* is considered to be an "NTR protein" because it encodes at least a portion of an NTR protein.

With regard to claims 30 and 66, Lalgudi *et al.* teach a nucleic acid that comprises a nucleotide sequence of SEQ ID NO: 10. This rejection applies to claims 30 and 66 only when claims 30 and 66 are interpreted to mean that comprising "**a** nucleic acid sequence" means that any nucleic acid which comprises any sequence from within those recited in figure 5A is encompassed within the claims (see 112 2nd paragraph rejection previously set forth).

With regard to claims 31 and 67, Lalgudi *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid having at least 75% sequence identity to a sequence as set forth in Figure 5A. This rejection applies to claims 31 and 67 only when claims

31 and 67 are interpreted to mean that "**a** sequence" refers to any sequence set forth within the figure, and not to the entirety of any of the three nucleic acids set forth in the figure or to SEQ ID NO: 10 in its entirety (see 112 2nd paragraph rejection previously set forth).

With regard to claim 32 and 68, Lalgudi *et al.* teach a recombinant nucleic acid encoding an amino acid sequence show in figure 4. This rejection applies to claims 32 and 68 only when claims 32 and 68 are interpreted to mean that "**an** amino acid sequence" refers to any sequence set forth within the figure, and not to the entirety of any of the three amino acid sequence set forth in the figure or to SEQ ID NO: 9 in its entirety (see 112 2nd paragraph rejection previously set forth).

With regard to claim 33, Lalgudi *et al.* teach a host cell comprising the nucleic acid (Col. 14, line 64).

With regard to claims 34, 73, 74, and 75, Lalgudi *et al.* teach an expression vector containing the nucleic acid operably linked to a transcriptional regulatory sequence (Col. 32, lines 63-67).

With regard to claims 35, 76, 77, and 78, Lalgudi *et al.* teach a host cell comprising an expression vector comprising the nucleic acid operably linked to a transcriptional regulatory sequence active in said host cell (Col. 33, lines 5-64).

With regard to claims 41, and 42, Lalgudi *et al.* teach a method of expressing an NTR protein comprising culturing the host cells of their invention under conditions suitable for expression of said protein (Col. 14, line 64-Col. 15, line 2).

With regard to claims 46, 91, and 94, Lalgudi *et al.* teach recovering said protein (Col. 15, lines 1-2).

Therefore, the teachings provided by Lalgudi *et al.* meet the limitations of the instantly rejected claims.

14. Claims 29, 30, 31, 32, 33, 34, 35, 41, 42, 46, 65, 66, 67, 68, 73, 74, 75, 76, 77, 78, 91, and 94 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacquot *et al.* (J. Mol. Biol. (1994) 235, 1357-1363).

This rejection applies to the rejected claims insofar as they are interpreted as referring to any of the three sequences given in instant figure 5A and 4. Jacquot *et al.* teach the nucleic acid encoding Arabidopsis thaliana NADPH-dependent thioredoxin reductase (NTR). Jacquot *et al.* teach that the isolated nucleic acid was disclosed as EMBL accession number Z23109 (p. 1358, Col. 1), which is included in this office action for applicant's convenience. The coding sequence of nucleic acid taught by Jacquot *et al.* is identical to the A. thaliana sequence provided in instant figure 5A, and encodes a polypeptide identical to the A. thaliana amino acid sequence provided in instant figure 4. Jacquot *et al.* refer to this nucleotide sequence throughout their paper as ATTHIREDB).

Thus, with regard to claims 29 and 65, Jacquot *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to instant a sequence taught in Figure 5A.

With regard to claims 30 and 66, Jacquot *et al.* teach a nucleic acid that comprises a nucleotide sequence of one of the nucleotide sequences taught in Figure 5A.

With regard to claims 31 and 67, Jacquot *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid having at least 75% sequence identity to a sequence as set forth in Figure 5A.

With regard to claim 32 and 68, Jacquot *et al.* teach a recombinant nucleic acid encoding an amino acid sequence show in figure 4.

With regard to claim 33, Jacquot *et al.* teach a host cell comprising the nucleic acid (E. coli host cells, p. 1360-1361).

With regard to claims 34, 73, 74, and 75, Jacquot *et al.* teach an expression vector containing the nucleic acid operably linked to a transcriptional regulatory sequence (p. 1361, Col. 1).

With regard to claims 35, 76, 77, and 78, Jacquot *et al.* teach a host cell comprising an expression vector comprising the nucleic acid operably linked to a transcriptional regulatory sequence active in said host cell (p. 1361, Col. 1).

With regard to claims 41, and 42, Jacquot *et al.* teach a method of expressing an NTR protein comprising culturing the host cells of their invention under conditions suitable for expression of said protein (p. 1361, Col. 1-2).

With regard to claims 46, 91, and 94, Jacquot *et al.* teach recovering said protein (p. 1361, Col. 1).

Therefore, the teachings provided by Jacquot *et al.* meet the limitations of the instantly rejected claims.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 36, 37, 38, 39, 40, 43, 44, 45, 69, 70, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90 92, and 93 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jacquot *et al.* in view of Shi *et al.* (Plant Molecular Biology 32:653-662, 1996).

Jacquot *et al.* teach the nucleic acid encoding Arabidopsis thaliana NADPH-dependent thioredoxin reductase (NTR). Jacquot *et al.* teach that the isolated nucleic acid was disclosed as EMBL accession number Z23109 (p. 1358, Col. 1), which is included in this office action for applicant's convenience. The coding sequence of nucleic acid taught by Jacquot *et al.* is identical to the A. thaliana sequence provided in instant figure 5A, and encodes a polypeptide identical to the A. thaliana amino acid sequence provided in instant figure 4. Jacquot *et al.* refer to this nucleotide sequence throughout their paper as ATTHIREDB).

Thus, Jacquot *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to instant a sequence taught in Figure 5A.

Jacquot *et al.* teach a nucleic acid that comprises a nucleotide sequence of one of the nucleotide sequences taught in Figure 5A.

Jacquot *et al.* teach a recombinant nucleic acid encoding an NTR protein comprising a nucleic acid having at least 75% sequence identity to a sequence as set forth in Figure 5A.

Jacquot *et al.* teach a recombinant nucleic acid encoding an amino acid sequence show in figure 4.

Jacquot *et al.* teach a host cell comprising the nucleic acid (E. coli host cells, p. 1360-1361).

Jacquot *et al.* teach an expression vector containing the nucleic acid operably linked to a transcriptional regulatory sequence (p. 1361, Col. 1).

Jacquot *et al.* teach a host cell comprising an expression vector comprising the nucleic acid operably linked to a transcriptional regulatory sequence active in said host cell (p. 1361, Col. 1).

Jacquot *et al.* teach a method of expressing an NTR protein comprising culturing the host cells of their invention under conditions suitable for expression of said protein (p. 1361, Col. 1-2).

Jacquot *et al.* teach recovering said protein (p. 1361, Col. 1).

Jaquot *et al.* do not teach transgenic plants which comprise the NTR encoding nucleic acids or constructs.

Shi *et al.* teach transgenic plants comprising recombinant nucleic acids encoding thioredoxins, as well as the seeds of these transgenic plants ("mature plants with pods") (p. 658). methods for transforming plants with thioredoxins (p. 654). Further, Shi *et al.* teach methods for expressing a thioredoxin protein which comprise culturing a plant comprising the recombinant nucleic acid under conditions suitable for expression of the thioredoxin (p. 654, 656), as well as methods of expressing a thioredoxin which comprise culturing transgenic seeds (p. 658). Shi *et al.* teach methods for recovering the expressed protein (p. 657-658).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have expressed the nucleic acid taught by Jaquot *et al.* in tobacco plants as taught by Shi *et al.* The ordinary practitioner would have been motivated to have produced transgenic plants expressing the NTR protein taught by Jaquot *et al.* in order to have provided an

alternative method to for the production of the NTR protein, since Shi *et al.* teach methods for producing an enzyme in transgenic plants and then recovering it using the FLAG epitope. Alternatively, the ordinary practitioner would have been motivated to produce plants expressing the NTR protein in order study the functioning of the NTR in plants since Gautier *et al.* since Jaquot *et al.* teach the NTR protein in plants has not been well characterized, as it had only been previously isolated from E. coli (p. 1358).

Conclusion

17. An isolated nucleic acid comprising instant SEQ ID NO: 10 is free of the prior art, as is an isolated nucleic acid encoding instant SEQ ID NO: 9.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Switzer whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Switzer
Examiner
Art Unit 1634

August 21, 2003